# SCIENCE

Vol. 90 — Friday, November 10, 1939 — No. 2341



SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKeen Cattell and published every Friday by

THE SCIENCE PRESS
New York City: Grand Central Terminal
Lancaster, Pa. — Garrison, N. Y.

Annual Subscription, $6.00 — Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington, D. C.

# CANCER AND THE PUBLIC HEALTH[1]

By Dr. THOMAS PARRAN, Jr.

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With parts or all of every continent at war, it is difficult even for neutrals to retain that dispassionate concentration upon *science* which is necessary for a fruitful discussion of the problems confronting this Third International Cancer Congress.

Devoting our lives, as we are, to the saving, the conservation of human life, it is inescapable that our first reaction to mass killing is one of frustration, of futility. How puny are our efforts to save compared with the effect of war. Four years of the World War nullified, wiped out, the results of probably forty years of medical progress. The lifetime of a hundred laboratories, a thousand scientists, tens, yes, hundreds of thousands of doctors and nurses gone for naught.

All of you, I am sure, share with me the fervent hope that we and our children will be spared the material, the physical, the mental, and above all the spiritual losses which follow a major conflict at arms.

Whether you thank or blame *science,* in these days no nation ever wins a war or profits by it—whether as a combatant or a neutral. Whatever its duration or costs, however, there is some consolation in the fact that every war is followed by peace.

Instead of becoming amateur strategists—as we are tempted to do—each of us must look forward even now to that peace, and consider in the meantime what we individually, in our chosen sector, can do to neutralize, to make up the losses which war entails.

Not counting other losses, if the material costs of the World War and the armament costs since then could have been spent to satisfy the basic needs of the people for peaceful living, the world to-day would be experiencing a standard of living beyond anything ever dreamed of. To attain a higher standard of national

[1] Address before the Third International Cancer Congress, Atlantic City, N. J., September 13, 1939.

health is an urgent need in this country—whether the future brings us continued peace or war.

In either event the nation can not afford the continued luxury of unnecessary disease, disablement and death. The public in this country is beginning to demand that its doctors and health organizations join hands to put their knowledge to work effectively—to prevent sickness, to improve health, to promote physical fitness, and to restore the sick to health.

The people have accepted the idea that a disease which takes a sweeping toll of lives each year from the productive ages of our population; a disease which knows no state or county boundaries; a disease which is so costly in its diagnosis and treatment that but few of its victims can pay the costs unaided—is a public health problem. Cancer is such a disease.

Each year more than 140,000 deaths from cancer occur in the United States—more than twice as many as live in Atlantic City. Irrefutable evidence indicates that skilled medical care is available only to a small proportion of the half million or more cancer sufferers in the United States to-day. Cancer death rates are highest among industrial workers and among the underprivileged economic groups.

There was a time when public health activities were limited to the control of epidemic diseases and basic measures to improve the sanitation of the environment. Health activities of to-day, however, are concerned with the prevention, alleviation, and cure of all of the major causes of disablement and death. Prompt restoration of the patient to health is equally important with the prevention of disease.

It is the realization among medical men of the *possibility* of *cure* for the cancer sufferer that motivates our modern cancer control activities. Some twenty-five years ago, professional groups and interested citizens joined to launch in the United States a movement which had as its objective the educating of physicians and the public to an effective understanding of the primary importance of early diagnosis and prompt expert treatment of cancer. This required a change in the traditional thinking of doctors. As has so frequently been the case in the advancement of health in this country, the private voluntary agency led the way to national action against cancer. The movement, initiated by the American Society for the Control of Cancer, has succeeded beyond expectations. Its future exceeds any of our present concepts.

Experience during the past twenty-five years, however, has clearly indicated that education alone is not enough to stem the mortality from cancer. We must know better how to prevent and cure it. Also, the advance of scientific knowledge and the improvement of technical skills and tools have placed cancer in the category of high-cost diseases. Organized services, special equipment and physicians highly trained in tumor pathology, radiology and surgery are the *sine qua non* of modern cancer therapy. For these reasons and because so many of the patients are unable to meet the costs of diagnosis and treatment, cancer has become one of our major health problems. Cancer deaths are increasing, and because of the aging of the population will continue to cause an increasing number of deaths if the present age-specific rates persist. Prior to 1937 only five states in the United States had recognized the importance of cancer as a public health problem, and had taken steps for the more wide-spread application of scientific knowledge of cancer. These states were: Massachusetts, New York, Connecticut, New Hampshire and Georgia.

An event possibly of great future significance in the growing anti-cancer movement in the United States was the passage by the Seventy-fifth Congress of the National Cancer Institute Act in August, 1937. Senator Homer T. Bone, who introduced the bill in the Senate, said at the laying of the cornerstone of the institute on June 24 of this year (1939): "Ninety-six members of the United States Senate attached their names to the bill creating this great institution. Never in the history of this Republic had the entire membership of either body of Congress sponsored a piece of legislation. Such an action reflected a great outpouring of sentiment and evidenced a grim determination to stamp out a disease that was threatening every home in America."

Two basic concepts underlie the Act: Research to develop more effective methods for the prevention and cure of cancer; and the better application of existing knowledge for the benefit of present cancer patients.

Experiments and investigations relating to the cause, diagnosis, and treatment of cancer are being conducted extensively. It is the function of the institute also to assist and foster approved research activities by other institutions, both public and private, by the distribution of funds and through cooperation.

Under the provisions of the National Cancer Institute Act, a National Advisory Cancer Council is created consisting of six members, selected from the ranks of leading medical or scientific authorities, who are outstanding in the study, diagnosis, or treatment of cancer in the United States.

This is a new venture in government policy. Never before has Congress authorized the distribution of tax funds to private institutions and individuals for medical research. We have been fortunate in the caliber of the members who thus far have served us on this council. Since so many scientific disciplines are important in the whole field of cancer research and treatment, it has not been possible to have representation of all of these disciplines on the council at any one time. We hope to seek advice and guidance broadly, however, from the various specialties concerned with

any aspect of this problem through the appointment of special committees of the council.

The council is in effect a policy-making body. Specifically it is authorized: (a) to review research projects or programs submitted to or initiated by it; (b) to collect, coordinate, and then disseminate the information with regard to cancer which is available or which will come to light as research and investigation progress; (c) to review applications from any university, hospital laboratory or other institution, whether public or private, or from individuals for grants-in-aid for research projects relating to cancer and certify its approval of grants-in-aid in such projects as show promise, and (d) to recommend the acceptance of conditional gifts to the National Cancer Institute.

To date, upon the certification of the council, grants-in-aid in excess of $180,000 for research projects have been made to various institutions throughout the country. Thus, in augmenting research and supporting worthwhile and promising cancer studies already being carried on by other agencies, the National Cancer Institute has taken its place in the world-wide attack on the cancer problem.

Two other important functions of the National Cancer Institute are provided in the Act, both of which have a direct relationship with the application of existing knowledge of cancer in the saving of lives: namely, the loan of radium and the training of professional personnel.

Under the provisions of the National Cancer Act, the Public Health Service is authorized to purchase radium and to make it available on loan to institutions, including hospitals, for cancer research or for the actual treatment of cancer. In 1938 nine and one-half grams of radium, costing $200,000, were purchased by the National Cancer Institute. The entire amount has already been allocated to various hospitals and cancer clinics. As funds become available, more radium will be purchased. It should be understood, however, that radium is *not* loaned *unless* an institution can meet certain requirements as to qualifications of the personnel, equipment and organization. The importance of this function of the institute can readily be appreciated when we consider the statements of experts when the Act was passed, that the United States possessed only about 50 per cent. of the radium needed for research and treatment of cancer.

Availability of competent personnel is also of great significance in the fight against cancer. Under the National Cancer Act, young physicians who are interested in cancer as a specialty and who have had previous training may apply to the National Cancer Institute for financial assistance in obtaining special training offered by designated training centers in tumor pathology, radiology and surgery.

Physicians eligible for training must be graduated from an approved medical school, must have completed at least one year of internship in an approved hospital, and must be less than 40 years of age. These fellowship appointments are made for one year, and are subject to renewal if the trainee's work is satisfactory. During the past year and a half, 36 physicians have received appointments.

Twenty-three institutions in the United States have been designated as centers where training and instruction may be given under a National Cancer Institute "traineeship," in all technical matters relating to the diagnosis and treatment of cancer. These institutions include nineteen leading schools of medicine and four outstanding hospitals devoted exclusively to tumor and cancer patients.

In compliance with another provision of the Act, the institute has endeavored through cooperative activities, to stimulate the interest of state health agencies in the promotion of cancer prevention and control. At the present time nine states—New Hampshire, Massachusetts, New York, Connecticut, Georgia, Missouri, Vermont, Pennsylvania and South Carolina—have cancer control laws. The cancer programs in Massachusetts, New York, New Hampshire, and Connecticut have been in operation for a number of years; those in Georgia, Missouri, Vermont, Pennsylvania and South Carolina are of more recent establishment, having been initiated during the past three years.

As a basis for cooperative services to other states, the National Cancer Institute has made an analysis of the effective cancer legislation in these nine states. The institute is now able to advise, upon request, as to the principles which should be considered in framing cancer legislation. In fact, upon the recommendation of the State and Territorial Health Officers at their annual conference with the Public Health Service, April, 1938, the National Cancer Institute has prepared a model bill for the guidance of the states. Upon request from state medical societies and state boards of health, the institute is prepared to give technical advice in regard to cancer control legislation.

Among other urgent needs for future advances in cancer research is an improvement in diagnosis and therapy, and a clarification of the present state of confusion surrounding cancer nomenclature and classification. The same unsatisfactory condition exists in regard to cancer record forms. To meet the need for uniformity of nomenclature and cancer case records, the National Advisory Cancer Council recommended the creation of a special committee to study these problems and to develop uniform nomenclature and uniform case records, including records of therapy and follow-up. Subcommittees have been formed. Organizations which are participating in the detailed study of these problems include: American College of Surgeons, American Board of Surgery, American Board

of Radiology, American Society for the Control of Cancer, Memorial Hospital in New York City and the Massachusetts Health Department.

It is probable that many months will have to be devoted to the solution of the problem engaging the interest of these experts. That the most advanced thought and the ablest advice will be brought to bear upon the questions under study goes without saying. Regardless of the time spent, we may confidently expect a satisfactory clarification of the perplexities connected with terminology and clinical records in the cancer field.

That the health of the people is a responsibility of government is no longer a question. Educators, statesmen and business men realize *now* that our greatest national assets are the human resources of the nation. Again and again, health departments, insurance companies and private agencies have demonstrated that no investment yields surer returns than expenditures for the prevention of disease and the care of the sick. For example, the Metropolitan Life Insurance Company has spent over a period of 30 years, 120 million dollars in health education, in nursing the sick and in the general prevention of disease. "We who are used to actuarial methods," says Dr. Louis I. Dublin, vice-president of the company, "are entirely satisfied with our investment. Year in and year out we have increased our investments in the preservation of health because we felt that these investments paid."

What the National Cancer Institute will eventually mean to the nation in the saving of lives may only be conjectured at this time. This will depend upon the extent to which it merits the confidence and cooperation of the scientific institutions, the medical profession and the people themselves. It is hoped that the benefits to the people, however, will be both direct and indirect; not limited to the present, but promising much for the future. The provision of a more adequate supply of radium for the treatment of present and future sufferers from cancer; the training of personnel for the correct diagnosis and appropriate treatment of the disease in its early stages are the more tangible and immediate benefits.

We have not the slightest doubt that some day, maybe soon, the cancer problem will be solved. There is no reason to be pessimistic about cancer research. It is not likely that any individual worker will singlehandedly conquer cancer. Scientific knowledge has increased and become so complex, that only through close coordination of research in the biological sciences with other disciplines can future advances in our knowledge of cancer be made. The National Cancer Institute of the Public Health Service hopes to demonstrate by the soundness of its policies, the extent of its cooperation and help, that it can attain an important place in this concerted warfare against the disease.

What we are discussing is no academic problem; cancer represents one important sector of a people's fight for life. You are engaged in a long-time struggle against one of mankind's oldest and most resourceful enemies; malignant growth of cells. If from this congress with its clashes of intellect and ideas, there should be generated the spark of understanding as to a means of ridding the world of the cancer menace, your contribution to humanity—to its happiness and future prosperity—might equal or even exceed the human losses of another world war.

On behalf of our government, therefore, I welcome your presence here. I wish you success in your deliberations. The one in ten of us in this country who, under the present rates, is doomed to die of cancer, pray that at least a beginning may be made toward unravelling the tangled skein, toward eradicating the menace of cancer.

# A NEW REACTION IN ORGANIC CHEMISTRY: THE REDISTRIBUTION REACTION

By Dr. GEORGE CALINGAERT

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THE chief difference between typical organic and inorganic compounds is the complete sharing of pairs of electrons in the bonds of the former, in contrast to the presence of electrostatic bonds in the latter. This results in profound differences in the behavior of these compounds. Electrostatic or ionic bonds are readily loosened in a suitable dielectric medium, such as water, for instance, and solutions result in which the two ions of opposite signs are in mass equilibrium with one another but where any one ion does not remain paired with one individual ion of the opposite sign. As a result, when two or more kinds of positive ions are introduced in a solution with two or more negative ions, separation of the salts from the solution will not necessarily yield back the particular salts which were originally introduced: the pairing of anions with cations will be governed primarily by solubility relationships, and appropriate manipulations of the conditions, primarily concentrations and temperatures, will effect predictable changes in the composition of these

recipitated salts. Accordingly, we should not think f a solution as containing, say, sodium ions in equilibrium with chlorine and bromide ions:

$$NaCl + KBr \rightleftarrows Na^{+} + K^{+} + Cl^{-} + Br^{-} \rightleftarrows NaBr + KCl.$$

The covalent bond, as the sharing of a pair of elecrons is called, is not readily dissociated either by soluion in a dielectric solvent or by heat or other means. hus, a solution of ethyl acetate and methyl butyrate ill contains these two compounds in the proportions n which they were introduced, and they can be readily ecovered unchanged by any appropriate method such s fractional distillation. In order to separate the two roups forming such a molecule, namely, the acid roup and the alcohol group, it is necessary to resort o chemical means whereby one of these groups is relaced by one of similar chemical nature but of greater eactivity; for instance, treatment of an ester with ulfuric acid will liberate the organic acid, while the ore reactive sulfuric acid then becomes combined ith the alcohol. If it is preferred to liberate the lcohol, a base such as sodium hydroxide may be used, n which case it is the organic acid which is obtained n combined form:

$$EtOAc + H_2SO_4 = EtOSO_3H + HOAc$$
$$EtOAc + HaOH = EtOH + NaOAc.$$

A new reaction has now been found whereby the lcohol and acid groups present in such a mixture of sters can be caused to exchange freely between the wo or more groups of the opposite type which are resent in the solution. Thus, the above mixture will ield two new compounds, namely, methyl acetate and thyl butyrate.

$$EtOAc + MeOBt \rightleftarrows MeOAc + EtOBt^{1}$$

his reaction takes place by the simple use of a catayst without the observable expenditure or production f energy, and practically without side reaction of ny kind. The result, therefore, bears a striking simiarity to the distribution of ions in an aqueous solution.

The reaction is not limited to esters, and similar obervations have been made in the case of alkyl halides uch as ethyl chloride and ethylene dibromide, and even ore strikingly in the case of organo-metallic comounds. The latter case is all the more remarkable ecause these compounds, in general, behave very much ke hydrocarbons, and their organic radicals can ardly be called functional groups, like the acid and lkyl groups in esters, or the halogens in alkyl halides, hich are all susceptible of being removed or reintroluced at will by the use of appropriate strong chemcal reagents. Typical examples of this reaction are llustrated in Figs. 1, 2 and 3, which show the distillaion curve of mixtures containing originally two comounds, and after reaction all the possible combinaions of the two kinds of radicals or atoms present.

[1] Ac = acetyl: $CH_3 \cdot CO-$; Bt = butyryl: $CH_3 \cdot CH_2 \cdot CH_2 \cdot CO-$.

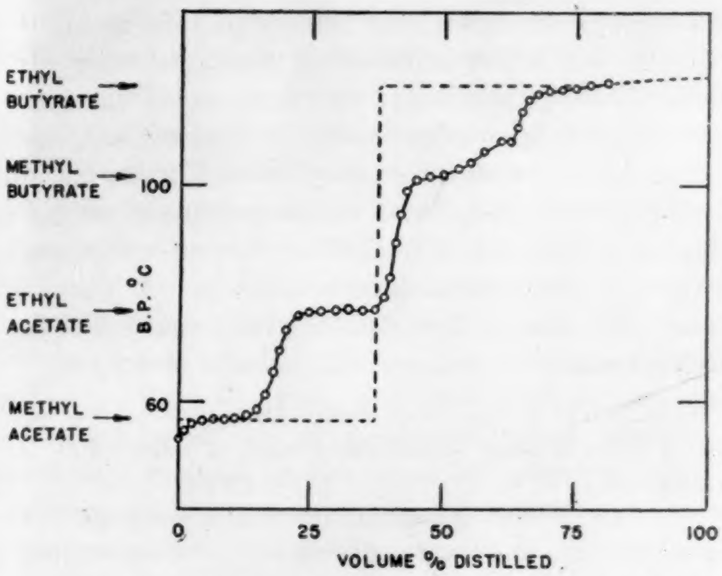


FIG. 1. Distillation of the reaction product of methyl acetate + ethyl butyrate. Dotted line represents distillation of same mixture before reaction.

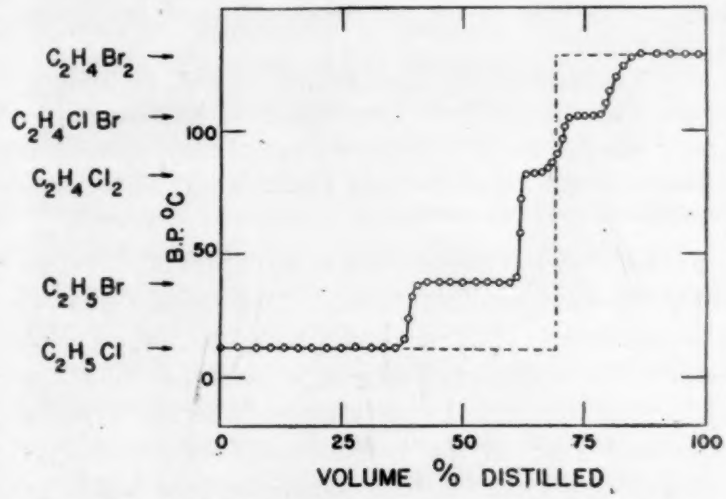


FIG. 2. Distillation of the reaction product of ethyl chloride + ethylene dibromide. Dotted line represents distillation of same mixture before reaction.

The organic chemist is apparently so steeped in the tradition that no reaction can take place between

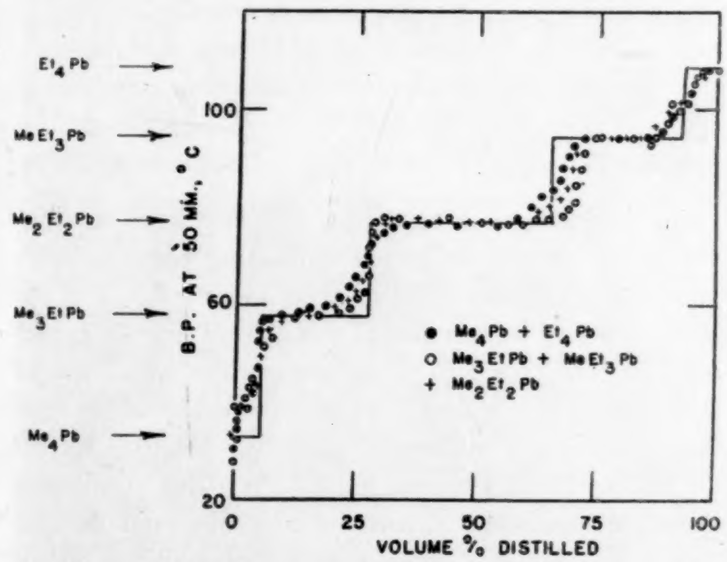


FIG. 3. Distillation of the reaction product of methyl and ethyl lead compounds. Solid line calculated for random equilibrium mixture having $r = 0.5$.

molecular groupings of the same type that no statement to that effect is found in the text-books; the notion becomes so obvious on the basis of our general chemical knowledge that it is subconsciously accepted. The present discovery seemed to strike so deeply at the foundation of our conception of organic chemistry that the investigation was soon directed toward an attempt to discern order in this seeming chaos. Systematic investigations have established the following characteristics of this unusual reaction:

(1) As far as has been ascertained, the reaction appears to be general within the classes of compounds investigated.

(2) The reaction is quantitative, and in some cases the most elaborate and precise methods of detecting by-products failed to find any.

(3) Little or no energy change is involved.

(4) The reaction is reversible, that is, the same final composition is obtained from any one or more starting materials as long as the bulk composition of the system is unchanged.

(5) The equilibrium composition is not appreciably affected by dilution with inert solvents, by temperature or any other commonly recognized independent variable in a chemical equilibrium, but is a function only of the gross composition of the system.

In view of the above observations, the simplest assumption was made regarding the nature of this equilibrium, namely, that it corresponded to the complete random distribution of the groups involved. The laws of probability express in simple form the expected proportions of all the possible combinations in systems of this kind. In the particular case which has been used most extensively for quantitative investigation in this field, namely, the case of tetraalkyllead compounds containing only methyl and ethyl groups, if we call $r$ the mole fraction of methyl groups in the mixtures of methyl and ethyl groups, *i.e.*, Me/(Me + Et), the concentration of the five possible compounds will be expressed by:

| | |
|---|---|
| $Me_4Pb$ | $r^4$ |
| $Me_3EtPb$ | $4\ r^3(1-r)$ |
| $Me_2Et_2Pb$ | $6\ r^2(1-r)^2$ |
| $MeEt_3Pb$ | $4\ r(1-r)^3$ |
| $Et_4Pb$ | $(1-r)^4$ |

Fig. 3 shows, as a solid line, the calculated distillation curve for such a system containing equal proportions of methyl and ethyl groups, *i.e.*, r = 0.5, and the three series of experimental distillation curves superimposed correspond to three systems for which $r = 0.5$ or nearly so, but in which the starting materials in each case were quite different, namely: $Me_4Pb + Et_4Pb$, $Me_3EtPb + MeEt_3Pb$ and $Me_2Et_2Pb$. Fig. 4 likewise gives corresponding calculated and observed distillation curves for two systems with high and low values of $r$, namely, $r = 0.345$ and $r = 0.776$. In each case, the agreement is remarkably good, showing that the distribution truly takes place completely at random.

These novel characteristics for a chemical reaction suggest the advisability of coining some new chemical terms and, accordingly, the reaction has been named "The Redistribution Reaction" and its final product a "Random Equilibrium Mixture."

The further investigation of the reaction was carried on principally in the field of organic metallic compounds, because these compounds react readily and with little or no side reaction and because the identity and exact concentration of the constituents of such systems are easily established.

Extended investigation of the reaction has shown it to take place in the case of alkyl or aryl groups, as well as with other metals than lead, such as tin, silicon and mercury, and complete random interchange of the radicals has been found to take place.

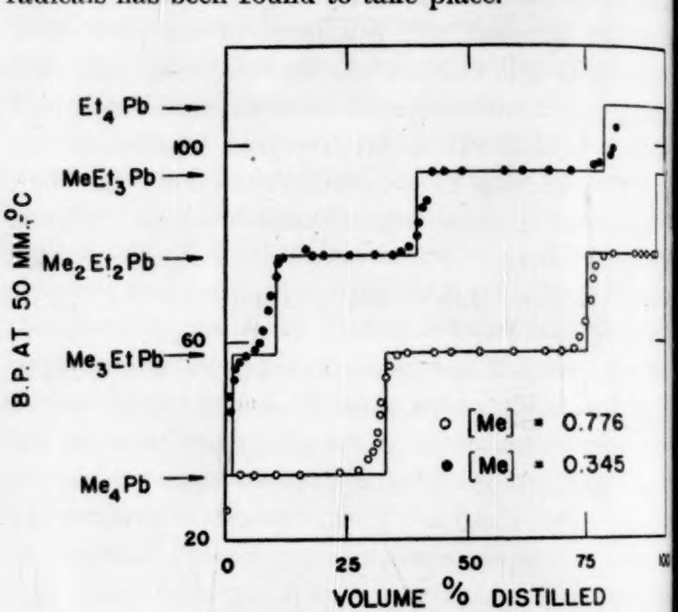


FIG. 4. Distillation of the reaction product of tetramethyllead + tetraethyllead. Solid lines calculated for ○ $r = 0.776$; ● $r = 0.345$.

Considering what we know of the instability of free radicals and their tendency to react with molecules or to rearrange yielding saturated and unsaturated hydrocarbons, it is remarkable to observe here a complete random mobility, without any loss of these groups through side reactions. This observed random distribution signifies that the bond strengths of the linkages involved are independent of the nature of the other linkages in the same molecule, that is, that the strength of a Me-Pb bond, for instance, is the same whether the other three linkages of the Pb are to methyl or to ethyl. This unexpected conclusion is likely to attract the attention of the chemists who spend considerable effort in attempting to determine bond strengths in atomic linkages. The systematic use of the redistribution reaction will be of considerable help in solving this key problem of molecular chemistry.

Another interesting application is in the study of relative affinities. When a system is investigated in which two or more groups of one kind, say alkyl

radicals in organo-metallic compounds, are redistributed between two or more different "acceptors," as we shall call them, such as lead and mercury, a new factor enters into play. In this case, methyl and ethyl radicals wander not only from one lead atom to another, but also from a lead atom to a mercury atom. Although, as it has just been stated, when only one metal is involved, the methyl bonds are not affected by the presence of ethyl bonds and conversely, there seems to be no reason to assume that the same will hold when two metals are present. In this case, a methyl radical attached to a lead atom may interchange with an ethyl radical attached to a mercury atom, and the two metals need not necessarily have the same relative affinity for the two alkyl radicals involved. This can be tested experimentally: If a random equilibrium mixture is made, for instance, containing equivalent quantities of methyl and ethyl radicals, on the one hand, and mercury and lead atoms on the other, in the absence of different affinity relationships, the observed methyl-ethyl distribution on each metal will be equal to the over-all distribution, namely, $r = 0.5$. A greater relative affinity of one metal for one radical will be reflected by a shift of the value of $r$ up for one metal and correspondingly down for the other. The equilibrium so obtained will obey the mass action law and give an equilibrium which is expressed by:

$$K = \frac{[\mathrm{Me-Pb}]\ [\mathrm{Et-Hg}]}{[\mathrm{Me-Hg}]\ [\mathrm{Et-Pb}]},$$

where the brackets denote the concentration of the corresponding bonds in the total product. The result of such an investigation on the Me-Et-Pb-Hg system is illustrated in Fig. 5, where the same final equilibrium

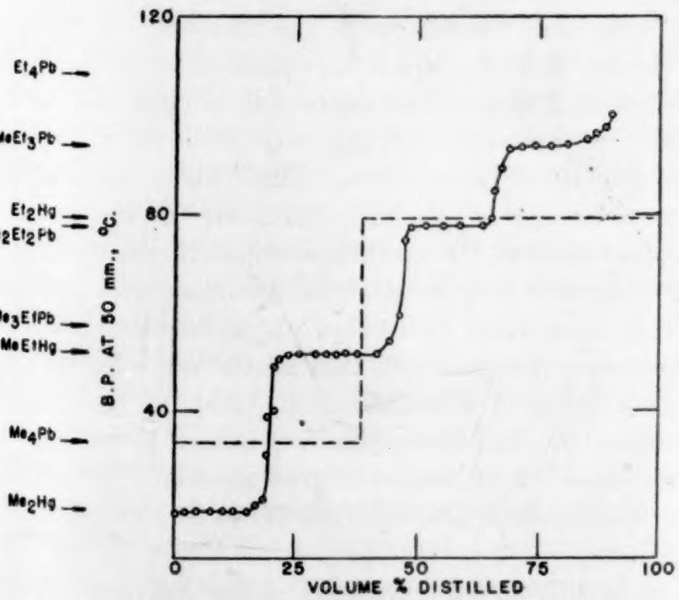


Fig. 5. Distillation of the reaction product from $Me_4Pb + 2\ Et_2Hg$, or $2\ Me_2Hg + Et_4Pb$. Dotted line represents distillation of the same mixture before reaction.

was reached from either end, that is, starting with $Me_4Pb + 2\ Et_2Hg$ as well as with $Et_4Pb + 2\ Me_2Hg$. By careful fractional distillation supplemented by analysis of each distillation cut for Pb and Hg, it was possible to tabulate the exact amount of each of the five lead and three mercury compounds formed. This corresponded in each case to a value of $r_{Pb} = 0.32$ and $r_{Hg} = 0.68$, giving a value of $K = 4.5$, showing that lead has a greater affinity for ethyl radicals, as compared to methyl, than has mercury.

Thus it is now possible by using the redistribution reaction to effect a direct measurement of the relative strengths of two kinds of bonds by actual observation under conditions of rigid equilibrium between the bonds involved, rather than by inference from the comparison of separate measurements, such as rates of reaction or the displacement of one radical by another.

The above quantitative observations clearly show the nature of the equilibrium. They throw, however, no light on the reasons for its existence or the mechanism involved. Reasoning by similarity with inorganic compounds, one might expect the mechanism to be through the formation of ions, while, on the other hand, the known existence of free radicals suggests the possibility of their playing a role in the redistribution reaction. Too much, however, is known about ions and free radicals as well as about the electronic nature of the covalent bond to make such explanations tenable. The organic compounds involved here are definitely not ionizable under the conditions used, and free radicals, if formed at all, would be bound to react with one another as well as with undissociated molecules, leading to the formation of large amounts of secondary products which are remarkably absent here.

The catalysts used in each case, although they may vary appreciably in chemical formulae, seem to have two characteristics in common, namely, (*a*) they contain one or more of the groups or atoms the redistribution of which they are capable of effecting, and (*b*) they are known or expected, on account of their electronic structure, to be capable of readily forming addition compounds with complete molecules of some kinds. This suggests that the mechanism of the redistribution reaction may be the reversible formation of a loose complex between a molecule of the catalyst and one or more molecules of the compounds to be redistributed. In this complex, the atoms or radicals to be redistributed are no longer identified with the particular molecule which has supplied them to the complex, but are shared in common by the residual parts of the catalyst as well as of the other molecule. When the complex breaks up, which probably occurs very frequently, each molecule, that is, the catalyst and the other compound, is reformed with its proper complement of groups, but these groups are taken at random from the common supply, and the final result of the repetition of this process is then the mathematical

equilibrium corresponding to complete random redistribution. This is represented schematically by the equation:

$$R_2R'_2M + R'C \rightleftharpoons [R_2R'_3]\ [MC] \rightleftharpoons R_3R'M + RC$$

in which R and R′ are the groups to be redistributed, M is the carrier, such as Pb in the case of alkyllead compounds, and R′C or RC is the catalyst.

The information obtained so far on the redistribution reaction is in accord with such a mechanism, but does not yet include data which confirm its correctness. Kinetic studies of the reaction and investigation of the physical and chemical characteristics of the catalyst are, however, expected to throw light on this point. It seems fair to expect that a closer scrutiny of the mechanism of the reaction will lead to a better understanding of the exact nature of the covalent bond and particularly of the exact mechanism whereby it is loosened and reformed in ordinary chemical reactions.

Beyond these positive studies one may well speculate whether this heretofore unsuspected reaction does not often take place spontaneously in natural systems containing several kinds of similar compounds. It may well be that the aging of alcoholic beverages is due at least in part to the redistribution of the esters to which they owe their flavor, while some of the little understood changes which take place in the living cell may correspond to the random interchange of the amino acid groups between the molecules of protein.

Practical applications should also not be overlooked. Two groups already suggest themselves at first sight. One is the preparation of mixed compounds such as mixed esters of polybasic acids, for instance: instead of preparing these by successive esterification, they can now be prepared directly by redistribution between the two corresponding symmetrical esters. A second and perhaps less obvious line would be the opening of new fields of use for materials heretofore considered too inert to be of practical value in chemical syntheses. For instance, organic bromides are not usually thought of as brominating agents because the bromine can not be removed by ordinary methods. As shown in Fig. 2, appropriate double decomposition between ethylene dibromide and an organic chloride will yield the corresponding bromide. Bearing in mind the availability and ease of handling ethylene dibromide, it seems probable that its use will prove advantageous in the preparation of some organic bromides, especially where the corresponding chloride is readily available.

The scientific reader who is not directly concerned with organic chemistry will be interested to note that this discovery carries a lesson which reaches well beyond the confines of its field. The concept of the absence of reaction between similar organic compounds has been accepted without challenge because of its usefulness in introducing order in our chemical knowledge. The experimental evidence reported above proves once more that we should ever bear in mind that the validity of any concept depends on how strictly we have been able to subject it to experimental verification and not on how long we have had it or how easily it fits our mental processes.[1]

[1] A complete technical report on the subject will appear in the *Journal* of the American Chemical Society beginning in October, 1939.

# OBITUARY

## WITMER STONE[1]

### (1866–1939)

WITMER STONE was born a naturalist, nurtured a naturalist, and a naturalist he lived to the end of his days. Most of the many activities that filled his busy life flowed from his profound interest in nature. An instinctive collector, he loved to gather about him the objects that excited his admiration and curiosity. In naming and classifying his specimens he became a systematist and a scientist. Inevitably as he made and mastered collections his keen perceptions discovered new kinds of animals and plants and new facts relating to kinds previously known. He wrote of his discoveries so wisely and so well that he became editor of the foremost ornithological journal of America. As a master editor and through his technical papers he became known throughout the world and added to his fame and that of the institution which was his scientific home.

Stone's association with the Academy of Natural Sciences of Philadelphia was practically life-long. It began in a boyish fascination following a visit to the museum when he was eight or nine years old and became closer year by year until 1888, when he assumed charge of the bird collections for the Ornithological Section. From this nominal official connection he succeeded step by step through curatorial positions from conservator to director of the museum. His life became so merged with that of the academy that for many years it was difficult to think of them apart. During the half-century of his official connection the collections of the academy grew greatly. The number of birds alone increased from 26,000 in 1888 to 143,000 in 1939.

Apart from his curatorial duties but more or less closely linked with them Witmer Stone's activities may be placed under four heads: namely, (1) scientific research, (2) nomenclatural, (3) editorial and histori-

[1] Based on a Minute of Appreciation presented to the council of the Academy of Natural Sciences of Philadelphia, October 3, 1939.

cal and (4) educational. To a remarkable degree he possessed the diverse attributes that made him successful in each. That these successes were somewhat notable is perhaps best indicated by the opinions of competent contemporaries, who so often designated the field of their own specialty as that in which Stone had excelled. There is a wide-spread agreement among ornithologists concerning the importance of his contributions under 2 and 3. His book reviews in the *Auk*, of which he wrote about 1,500, are famous and widely read. Except for his "Bird Studies at Old Cape May," his papers on moult, plumages and migration and his "Plants of Southern New Jersey," his research publication seems to be less read, but its good quality is unquestioned. Concerning the value of his informal but effective educational influence, there is almost universal agreement. It was effected chiefly through direct personal contact. One prominent ornithologist writes, "I have never heard him open his mouth, either in private conversation or public speech without saying something significant and worthy of attention."

In each of his several activities Dr. Stone became by sheer ability and industry a recognized leader. He was a founder or a constructive member of several important biological societies. He became president or vice-president or both of the American Ornithologists' Union, the Delaware Valley Ornithological Club, the American Society of Mammalogists, the Philadelphia Botanical Club and the Pennsylvania Audubon Society. He was a vice-president of the Academy of Natural Sciences of Philadelphia and could have become president, following the death of Dr. Samuel G. Dixon, had he not declined. He was secretary of the Ludwick Institute since 1920 and a manager of the Philadelphia Zoological Society. Of the famous University of Pennsylvania Class of '87 he was secretary from undergraduate days to the time of his death. Many other unsought honors came to him. The University of Pennsylvania conferred upon him the Sc.D. and the Alumni Award of Merit. The National Committee of Audubon Societies established the Witmer Stone Wild Life Sanctuary at Cape May. The Hungarian Ornithological Society awarded him its Otto Hermann Medal and the American Ornithologists' Union its Brewster Medal posthumously. No other person received so many honors from the latter society as did he. Dr. Stone was elected to honorary or equivalent membership in many important foreign ornithological societies. After twenty years as editor of the *Auk* some 130 fellows and members of the American Ornithologists' Union presented him with a volume of testimonial letters, and on his seventieth birthday he was presented with a similar tribute from friends. The letters express the esteem in which he is widely held. When our front-rank ornithologists apply to him such terms as "dean of American ornithologists," "master workman in ornithology" and the like, it means that we have lived in the presence of a man of exceptional merit.

It may be permissible to venture a description of the historical niche in American ornithology which Witmer Stone occupies. Briefly, North American ornithology may be divided roughly into four periods. First was the pioneer period when the birds of the eastern United States were discovered and described. Second was the period of exploration and government surveys of the West, extending our knowledge of birds to the Pacific. Third was a period of consolidation and systematization, of organized effort, largely through the American Ornithologists' Union, to eliminate confusion by the adoption of exact concepts of species and subspecies and the attainment of a stable nomenclature. Dr. Stone was a dominant figure during much of this period, and its close may be placed in 1931 with the publication of the fourth edition of the A. O. U. Check List. One ornithologist has designated it as the "Stone Age" of American ornithology. Due to the arduous labors of Stone and his contemporaries it forms a solid foundation for the precise studies of the fourth or present period.

Of Dr. Stone it may be said that the seed within him on fertile soil grew into a sturdy tree of many branches, bearing fragrant flowers and nourishing fruit. Naturalist, scientist, faithful custodian of collections, biographer and historian of scientists and their science, interpreter of the rules of zoological nomenclature, protector of birds, writer of exceptional beauty and vigor, sometimes poetical, lecturer and teacher, helpful adviser, delightful companion and valued friend, Witmer Stone gave the best of his life and labor to this historic academy and of the riches of his personality to colleagues and associates.

His works and our memories are a fitting memorial, and may his spirit long abide in the lives of those on whom he spent it.

## RECENT DEATHS

DR. FLOYD KARKER RICHTMYER, professor of physics and dean of the graduate school of Cornell University, died on November 7 at the age of fifty-eight years.

DR. WALDEMAR LINDGREN, from 1912 until his retirement with the title emeritus in 1933 Rogers professor of economic geology at the Massachusetts Institute of Technology, died on November 4 at the age of seventy-nine years.

DR. FRANK ANGELL, emeritus professor of psychology at Stanford University, died on November 2 at the age of eighty-two years.

DR. ROBERT MACDOUGALL, emeritus professor of analytical psychology at New York University, died on October 31 at the age of seventy-three years.

DR. JOSEPH B. LINDSEY, from 1911 to 1927 head of the department of chemistry at the Massachusetts State College and from 1911 to 1932 Goessmann professor of agricultural chemistry, died on October 27 at the age of seventy-seven years.

DR. WILLARD BURR SOPER, associate professor of medicine at Yale University and medical director of the William Wirt Winchester Hospital, the tuberculosis unit of the New Haven Hospital, died on October 30 at the age of fifty-six years.

COLONEL GUSTAV J. FIEBEGER, Corps of Engineers, who for twenty-six years was head of the department of civil and military engineering of the United States Military Academy at West Point, died on October 18 at the age of eighty-one years.

# SCIENTIFIC EVENTS

## THE GALTON LABORATORY

DR. R. A. FISHER, Galton professor of eugenics at University College, London, writes under date of September 29 the following letter to the editor of the London *Times:*

The evacuation of London University has been represented as carefully planned and smoothly carried out in accordance with prior arrangements, and I am sure that the central officials of this loose federation have done what they can in difficult circumstances. The position in which the Galton Laboratory finds itself may be typical of other research departments in the university, or it may be, as I hope, exceptional, but it is scarcely what could have been intended by the careful planners.

The laboratory was founded on a generous bequest of the benefactor whose name it bears, and has, I presume, an unquestioned right to the provision of facilities for the prosecution of its researches. Nevertheless it has been ordered to evacuate the accommodation it now occupies at University College without alternative accommodation being provided. Worse than this, when in my difficulty I approached my former chief, Sir John Russell, Director of the Rothamsted Experimental Station, and he had helpfully and generously offered to provide alternative accommodation for my department and equipment rent free, I was informed that my assistants, while still in receipt of their salaries, are forbidden to continue their duties.

As the head of this department, therefore, the only determined policy which I can recognize on the part of the College Committee is that of suppressing research work and dispersing the research units such as that which it has been my work and, as I understood it, my duty to build up.

During the last war our administrators learned, though perhaps with some reluctance, that men trained in research were essential for the success of the national effort. The remaining nucleus of my department, if I may speak in its praise, constitutes a unit for heavy mathematical computations as efficient, both in machines and men, as the country can command. Obviously no work of first-class national importance can be found for such a unit at a few days' notice. I submit that it is almost equally obvious that in certain contingencies its continued existence might be of the greatest value, so long as the machines and the expert knowledge had been kept together. Can not a little patience be exercised before completing its demolition?

## THE PRIVATELY ENDOWED COLLEGE OF ENGINEERING

A BROADCAST sponsored by the alumni of the Case School of Applied Science was made on October 28 for consideration of the question, "What's Ahead for the Privately Endowed College of Engineering?" The program, which was given at a luncheon of the alumni in Cleveland, was carried nationally over the Mutual Broadcasting Company's system.

The consensus of opinion of the six participants in the radio discussion was that engineering colleges which depend on endowment and gifts need additional funds to overcome the decline in earnings from investments and to provide for new educational services. These funds should be sought from those benefited, directly or indirectly, from the work of the colleges, These comprise the alumni, industry, which depends on these colleges for their trained personnel, and society, which profits from the earnings of industry. The reasons why so few large gifts have been made to colleges of technology is due, the conferees believed, because of the inactivity of these institutions in placing their needs before persons of wealth.

Participants in the radio discussion were leaders in industry and scientific men, all residents of Cleveland. The speakers were: George S. Case, chairman of the board, Lamson and Sessions Company; Lee M. Clegg, executive vice-president, Thompson Products Company; David Dietz, science editor, Scripps-Howard Newspapers; Randolph Eide, president of the Ohio Bell Telephone Company; Sam W. Emerson, president of the S. W. Emerson Company, contractors, and Dr. Zay Jeffries, technical director, Lamp Department, General Electric Company.

In summing up the problem of getting funds for technological education, Dr. William E. Wickenden, president of the Case School of Applied Science, said:

Traditional motive makes it much easier to get money for religion, for hospitals, for medical research and for the fine arts, than for science and engineering. Our graduates are giving splendidly, out of loyalty, but I wonder if our big job is not to implant new motives in the minds of wealthy men.

One such motive is this: No man, no company, no industry can do business to-day without the aid of the priceless heritage of science and skill which has come down to it all the way from Tubal Cain to Arthur Compton without a cent of direct cost. Take away Faraday's work and where would the electrical industry be? There's a moral debt to be paid, and the best way to pay it is through the schools of applied science. Then, too, much of to-day's wealth is coming from natural resources we can never replace. Every pound of coal or iron, every gallon of oil, every foot of natural gas we consume makes it just that much harder for our children and their children to make a good life. This is going to hit Cleveland, which owes so much of its wealth and greatness to these resources, unless it builds up resources in science and skill to take their place. That is the way to make good to the future for what we are using up to-day, to build up science and skill.

An institute of applied science, such as Case, really asks nothing for itself. Every cent goes back to the community and the nation with its value multiplied, to make to-day's living better and to-morrow's future more secure.

## THE AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

DR. FRANK R. SPENCER, of Boulder, Colo., was chosen president-elect of the American Academy of Ophthalmology and Otolaryngology at the annual session held in Chicago on October 11. He will succeed Dr. Frank E. Brawley, of Chicago, when the latter becomes president of the academy on January 1. Dr. Spencer is a graduate of the University of Michigan Medical School and has been a member of the faculty of the University of Colorado School of Medicine since 1905.

The academy decided to act as sponsor for a proposed Pan American congress of ophthalmology and otolaryngology. South American physicians attending the meeting in Chicago will arrange for the attendance of delegates from their respective countries to such a congress to be held in connection with the next meeting of the academy. It is understood that invitations to each of the countries concerned will have the sanction of the Department of State and will be forwarded through diplomatic channels.

Other officers elected were Drs. Arthur W. Proetz, St. Louis, *first vice-president;* Joseph F. Duane, Peoria, Ill., *second vice-president,* and Charles T. Porter, Boston, *third vice-president;* Secord H. Large, Cleveland, *comptroller,* and William P. Wherry, Omaha, Nebr., *executive secretary,* reelected. Dr. Erling W. Hansen, Minneapolis, was elected secretary for public relations, succeeding Dr. Ralph A. Fenton, Portland, Ore., who resigned. The following secretaries were reelected: Drs. William L. Benedict, Rochester, Minn., for ophthalmology; John L. Myers, Kansas City, Mo., for otolaryngology; Dean M. Lierle, Iowa City, for instruction in otolaryngology, and Albert D. Ruedemann, for instruction in ophthalmology. Dr. Albert C. Snell, Rochester, N. Y., was elected a member of the academy's governing council, and Dr. Frederick C. Cordes, San Francisco, to represent the academy on the American Board of Ophthalmology.

The academy continued the following appropriations for research: Dr. Olof Larsell, University of Oregon Medical School, Portland, $400 for research on development of the internal ear; Dr. M. H. Lurie, Harvard Medical School, Boston, $400 for research on the balancing apparatus of the ear, and for the Army Medical Museum at Washington, D. C., $1,500 for maintaining collections of pathological specimens in diseases of the eye, ear, nose and throat. An appropriation of $1,500 was also made for the establishment under the supervision of the academy of reading courses for young physicians serving as residents in hospitals who are preparing for specialization in diseases of the eye, ear, nose and throat. A grant of $400 was made to Dr. Spencer for research on the action of drugs on tubercle bacilli in the nose and throat. The committee on physiological optics received $50 and the committee on orthoptics $200.

## SCIENTIFIC EXPEDITIONS

THE expedition sponsored by the National Geographic Society and the University of Virginia with the U. S. Coast Guard cooperating, which was to have sailed from San Francisco on September 19 on the Coast Guard cutter *Hamilton* has been postponed. The *Hamilton* has been ordered to Atlantic waters as part of the coast patrol. In preparation for the expedition tons of scientific equipment had been shipped to the Pacific Coast to be loaded on the *Hamilton,* and members of the expedition had spent months of intensive work in preparing apparatus for studying geology, magnetism of the earth, variations in gravity, earthquakes, marine biology, weather, ocean currents, and for collecting samples of the ocean bottom from great depths. The expedition was planned to conduct the most extensive program of scientific work so far attempted in the region of the Pacific Islands. Professor Wilbur A. Nelson, leader of the expedition, is returning to his work as professor of geology at the University of Virginia, to await conditions better suited to scientific research on the high seas.

THE second Fahnestock expedition to the South Seas of the American Museum of Natural History, organized by Bruce and Sheridan Fahnestock, will leave New York in the near future in the three-masted auxiliary schooner *Director II.* In addition to collecting material for six habitat studies for the new Whitney Memorial Bird Hall and specimens of fish, insects and minerals, islands out of position on existing charts will be remapped. It is expected that the ex-

pedition will take from eighteen months to two years. Later an entomologist, a geologist and a recording technician will be appointed from the American Museum staff and from Columbia University.

A SIX months' expedition to make a comprehensive collection of the plants of Guatemala for the herbarium of the Field Museum of Natural History left Chicago on September 27 under the direction of Dr. Julian A. Steyermark, assistant curator of the herbarium, who sailed on the steamship *Ulm* from New Orleans. The expedition is sponsored by Stanley Field, president of the museum. It is planned to explore the little known Oriente area in the departments of Chiquimula, Jutiapa and Jalapa. Work in the desert area around Zacapa will be carried out during the rainy season, and Dr. Steyermark expects to find a number of unusual species of plants. The expedition then plans to move into the Sierra Madre region of western Guatemala, in the provinces of San Marcos and Huehuetenango. Particular attention will be devoted to the flora of the Tajumulco volcano, and collecting is contemplated in the district around Mazatenango.

### FIELD WORK OF THE U. S. GEOLOGICAL SURVEY

AMONG the members of the Geological Branch who have recently returned to Washington, D. C., after completing their season's field work on the projects indicated, are the following:

S. R. Capps, who studied the structural history of west-central Idaho in its relation to the gold placer deposits.

H. G. Ferguson, who continued studies of structural and stratigraphic problems in Nevada and completed preliminary mapping of the western and central parts of the Sonoma Range quadrangle.

T. A. Hendricks and Paul Averitt, who investigated the geology and oil possibilities in the western part of the Ouachita Mountains, Okla.

A. A. Baker, who studied the phosphate and coal resources and oil and gas possibilities in the southern Wasatch Mountains, Utah.

W. P. Woodring, who examined the geology and oil resources in the Santa Maria district, Calif.

W. C. Warren, who, with the aid of aerial photographs, mapped about 1,150 square miles of coal lands in southeastern Montana.

D. A. Andrews, who completed his fourth season of study of the stratigraphy, structure, economic geology and geomorphology along the northeast flank of the Bighorn Basin, Wyoming and Montana.

C. B. Hunt, who completed his fifth and final season of investigating the geology of the Henry Mountains, Utah, and examined gold placer gravel deposits and unusual erosion features in the canyon of the Colorado River between Hite and Lee's Ferry.

Members of the Alaskan Branch have completed the season's field work in Alaska and have returned to Washington for the office and laboratory studies required to put their resulting maps and notes into shape for publication. F. H. Moffit examined the east-central part of the Alaska Range, embracing principally the country between Delta and Johnson Rivers. J. C. Reed carried on geological surveys in the northwestern part of Chichagof Island, southeastern Alaska. J. B. Mertie, Jr., investigated the potential tin fields of western Seward Peninsula. Gerald Fitzgerald made extensive topographic surveys in the vicinity of Porcupine River from Fort Yukon to the Canadian Boundary. T. V. Ranta revised much of the early exploratory mapping of the country between Nabesna and Chisana Rivers, near the head of Tanana River. Philip S. Smith inspected a number of the more accessible mining districts in central Alaska, and collected information as to new mining developments in progress.

## SCIENTIFIC NOTES AND NEWS

THE Royal Society, London, according to a wireless report in *The New York Times,* awarded on November 2 the Copley Medal to Professor Thomas H. Morgan, director of the William G. Kerckhoff Laboratories of the California Institute of Technology, for his work in genetics, and the Davy Medal to Dr. James W. McBain, professor of chemistry at Stanford University, for his work in colloid chemistry.

THE Sedgwick Memorial Medal, awarded for distinguished service in public health, was presented to Dr. Thomas Parran, Jr., Surgeon General of the United States Public Health Service, on October 17 at the sixty-eighth annual meeting of the American Public Health Association in Pittsburgh. Dr. Milton J. Rosenau, director of the Division of Public Health of the School of Medicine of the University of North Carolina, made the presentation.

DR. FRANCIS CARTER WOOD, director of the Institute of Cancer Research of Columbia University, was presented with the Clement Cleveland Medal for 1939 at the annual dinner of the New York City Cancer Committee.

A CITATION for distinguished service to agriculture was presented to Dean Emeritus F. B. Mumford, of the Missouri College of Agriculture, at the annual banquet on November 2 of the Association of Alumni and Former Students. The banquet was held on the last evening and formed part of the centennial celebration of the university.

The Charles Frederick Chandler Medal of Columbia University will be presented to Thomas Hamilton Chilton, director of the Technical Division of the Department of Engineering in the E. I. du Pont de Nemours and Company, on the evening of November 16, when Mr. Chilton will deliver the annual Chandler Lecture. His subject will be "Engineering in the Service of Chemistry."

According to press reports the Nobel Prize for physiology and medicine "has been regretfully declined" by Professor Gerhard Domagk, director of the research institute of the I. G. Farbenindustrie Laboratory at Elberfeld. It is said that he has written to the Stockholm committee, thanking them for the honor conferred on him, but pointing out that under the present law no German is allowed to accept a Nobel Prize.

Sir Charles Sherrington, Waynflete professor of physiology at the University of Oxford, has been elected to an honorary fellowship in Magdalen College.

Arthur Nutt, vice-president for engineering of the Wright Aeronautical Corporation, has been nominated for the presidency of the Society of Automotive Engineers.

Dean Olin J. Ferguson, of the College of Engineering of the University of Nebraska, has been elected president of the Society for the Promotion of Engineering Education for the year 1930–40. He succeeds Dr. Karl T. Compton, president of the Massachusetts Institute of Technology. The secretary is Dr. F. L. Bishop, of the University of Pittsburgh. The annual meeting will be held at the University of California from June 25 to 28, when it is expected that a thousand delegates will be in attendance.

Professor Frank Cyril James, director of the School of Commerce of McGill University, will succeed Dr. Lewis W. Douglas as principal and vice-chancellor of the university. Mr. James, a native of London, is thirty-six years old and is a British subject. In 1924 he was appointed instructor of finance in the Wharton School of Finance and Commerce of the University of Pennsylvania, becoming full professor in 1935.

Dr. George W. Corner, since its establishment in 1924 professor of anatomy and chairman of the department in the School of Medicine and Dentistry of the University of Rochester, has been appointed director of the department of embryology at the Carnegie Institution of Washington. He succeeds on May 1, 1940, Dr. George L. Streeter, who since 1917 has been director of the department.

Kenneth H. Condit will succeed Professor Arthur Maurice Greene, Jr., as dean of the School of Engineering of Princeton University, Professor Greene, since 1922 dean of the school, having presented his resignation. Mr. Condit is at present assistant to the president of the National Industrial Conference Board. He was elected at the recent annual meeting vice-president of the American Society of Mechanical Engineers.

Dean William H. Hall has been made head of the new college of engineering at Duke University.

Dr. Wilber E. Post, for the past twenty years clinical professor of medicine at the Rush Graduate School of Medicine of the University of Chicago, has been appointed dean.

Dr. Howard Y. McClusky, of the University of Michigan, has been promoted to a professorship of educational psychology, mental measurements and statistics. He has also been made assistant to the vice-president in charge of university relations in the field of adult education.

Dr. Leroy A. Schall, who has been instructor in laryngology at the Harvard Medical School since 1926, has been appointed Walter Augustus Lecompte professor of otology and professor of laryngology. He succeeds Dr. Harris P. Mosher, who has taught at the Medical School for more than thirty years and now becomes professor emeritus.

Dr. S. Ulam has been appointed lecturer in mathematics at Harvard University for the academic year 1939–40.

Dr. Pettus Holmes Senn, of the department of agronomy of the University of Florida, has been promoted to a professorship of agronomy and to the head of the department in the teaching division of the College of Agriculture.

Department chairmen at Queens College, New York City, who are elected by the faculty, have been chosen in the science departments as follows: Professor Donald E. Kirkpatrick, physics; Professor Anne Anastasi, psychology; Dr. John Dambach, health and recreation; Professor T. Freeman Cope, mathematics; Professor Roland Whittaker, chemistry; Dr. Hortense Powdermaker, anthropology and sociology, and Professor Donald E. Lancefield, biology. The appointments will be presented to the Board of Higher Education for formal approval.

Dr. Eliot G. Mears, professor of geography and international trade at Stanford University, will be the general chairman of the seventeenth annual Institute of World Affairs, to be held under the auspices of the University of Southern California at the Mission Inn, Riverside, Calif., from December 10 to 15.

Dr. Detlev W. Bronk, director of the Eldridge R. Johnson Foundation for Medical Physics and of the Institute of Neurology of the University of Pennsylvania, has been appointed managing editor of *The*

*Journal of Cellular and Comparative Physiology* of the Wistar Institute of Anatomy and Biology, Philadelphia. He succeeds Professor E. Newton Harvey, of Princeton University.

SIR JOSEPH BARCROFT, from 1926 until his retirement in 1937 professor of physiology at the University of Cambridge; Sir Harold B. Hartley, chairman of the Fuel Research Board of the Department for Scientific and Industrial Research, and Sir Frank E. Smith, secretary of the department and a secretary of the Royal Society, have been appointed members of the Advisory Council to the Committee of the Privy Council for Scientific and Industrial Research. Lord Cadman and Sir James Jeans have retired from the council on completion of their terms of office.

DR. FOREST RAY MOULTON, permanent secretary of the American Association for the Advancement of Science, addressed members of the Academy of Medicine of Washington, D. C., on the evening of October 27. The title of his address was "A Jaundiced Look at the Human Machine."

DR. C. STUART GAGER, director of the Brooklyn Botanic Garden, gave an address at the three hundredth meeting of the Botanical Society of Washington, D. C., on November 7. His subject was "How Botany Advances." The address was preceded by "illustrated reminiscences," with portraits of former botanists of Washington.

DR. ELLIOTT C. CUTLER, Moseley professor of surgery at the Harvard Medical School, spoke before the Omaha Mid-west Clinical Society in Omaha on October 26 on "Incomplete Intestinal Obstruction" and on "Acute Appendicitis." On October 30 he spoke on the "Surgical Treatment of Gallstones" at the Inter-state Post-graduate Medical Assembly of North America in Chicago.

THE first of the 1939–40 series of Foster Lectures at the University of Buffalo was given on October 26 by Dr. Vincent du Vigneaud, professor of biochemistry at the Cornell University Medical College, New York City. His subjects were "The Metabolic Relationship of Choline and Methionine" and "Tracing Chemical Reactions in the Body by Means of Isotopes." During the week of November 13, Professor Kasimir Fajans, of the University of Michigan, will be in residence. He will give six lectures on the chemical aspects of crystal structure, adsorption indicators, types of chemical linkages, and refractometric investigations. The Foster lectures are provided by the proceeds of a fund given the university by the late Mrs. O. E. Foster in memory of her husband.

THE program for the New England Conference of the American Association of Museums at the Springfield Museum of Fine Arts has been arranged in outline, according to *Museum News*, as follows: Friday, November 24, registration, address of welcome and a business meeting; a special performance in the planetarium for delegates, followed by tea and a subscription dinner, with an address by Andrey Avinoff, director of the Carnegie Museum, Pittsburgh, on "The Relationship of Science and Esthetics in the Museum." Saturday, November 25, morning sessions by art and science groups meeting separately; a special program for the art group in connection with an exhibition of paintings and drawings by David and Ingres; luncheon at the museum; a joint session, at which questions raised by Mr. Avinoff's address will be discussed, and a tea and a gallery talk by Katherine Dreier in connection with the first showing of the collection of the Société Anonyme.

THE recently formed Sigma Xi Club of Hawaii held its first annual meeting in the new Union Building of the University of Hawaii on October 20. The election of thirteen new members raised the membership total to sixty-five. Officers elected for the ensuing year were: *President,* Dr. C. J. Hamre, associate professor of zoology in the University of Hawaii; *Vice-president,* Dr. Martha Potgieter, associate nutritionist in the Hawaii Agricultural Experiment Station; *Secretary-Treasurer,* Dr. S. S. Ballard, assistant professor of physics in the University of Hawaii; *Councilors,* Dr. H. E. Gregory, retired director of the Bernice P. Bishop Museum, and C. E. Pemberton, executive entomologist of the Experiment Station of the Hawaiian Sugar Planters' Association. The address of the evening was delivered by Dr. Hamre, who spoke on "Some Aspects of the Physiology of the Bone Marrow."

IN a statement made by Chancellor O. C. Carmichael, of Vanderbilt University, it is announced that more than $1,500,000 of a bequest from the estate of Frederick W. Vanderbilt has been received by the university.

BY the will of the late Henry W. Putnam, a New York manufacturer, who left an estate valued at over $21,000,000, Harvard, Yale and Princeton Universities will share the sum of $9,858,332 upon the death of four of his cousins. The sum of $3,000,000 is bequeathed to the Henry W. Putnam Memorial Hospital at Bennington, Vt.

ACCORDING to a press dispatch from Pasadena, Dr. John Martin Vincent, emeritus professor of European history in the Johns Hopkins University, who died in September at the age of eighty-one years, left his estate, said to be of the value of $1,500,000, to the department of history.

THE will of the late Richard Halliburton, the explorer, leaves an estate, believed to be worth about

00,000, largely in trust to his parents with the pro- ion that, following their death, it be turned over to inceton University to establish a Richard Hallibur- Geological Library.

THE five million kronen collected on the occasion of e thirtieth year of the reign of King Gustaf of veden will be devoted to the establishment of a foun- tion for the study of paralytic diseases, especially liomyelitis, and to the campaign against tubercu- is.

FORMAL exercises dedicating the Medical Building the University of North Carolina will be held on ecember 4. The morning will be devoted to ad- esses by prominent physicians and experts in public alth. The afternoon will be given over to inspection of the new building, and a banquet in the evening will conclude the program.

AN Associated Press dispatch states that further Nobel Prize awards will be withheld this year, due to the European war. The literary, physics and chemistry prizes for 1939 may be awarded next year, but the 1938 chemistry prize, postponed last year, will be permanently omitted and the prize money, about $38,-769, returned to the main fund.

THE Statistical Laboratory of the Iowa State College, of which Professor G. W. Snedecor is director, has recently made an agreement with the Bureau of Agricultural Economics of the U. S. Department of Agriculture to provide for joint research in the statistics of agriculture and associated statistical theory.

# DISCUSSION

## VITALIZING HISTORICAL GEOLOGY THROUGH FIELD TRIPS

FIELD trips, if they are to constitute a part of a urse in general geology, should make a vital con- ibution to the course. It frequently happens that this ntribution can be made more easily when the work als with physical geology than when it deals with storical geology. Since one or more of the geologic ents are continually at work in any given region it not difficult to plan a field trip on which the student n observe some of the physical processes which they dy in class. In some regions it is a little more diffi- lt to plan a field trip that will make a vital contri- tion to the study of historical geology. In some calities only a limited geologic column is accessible to e students without the expenditure of an unreason- le amount of time and money. In such cases the ld trip may resolve itself into a fossil-collecting pedition or a superficial study of the rocks of the gion with little or no connection with the work of e classroom.

For several years the author has been attempting remedy this weakness and to make the field work of s students contribute more than that to their work general geology. An article recently published by wynne[1] describing his efforts to make the field trip real teaching device, suggested to our mind that the an we had tried this year might be interesting and lpful to other geology teachers.

It so happens that the rocks in the region around ew Concord are in the Conemaugh series of the ennsylvanian system. Most of the ridges of the re- ion are high enough to include the lower part of the onongahela series. Since this is the case it seemed desirable to make an effort to correlate the field trips with our class discussion of the Pennsylvanian system.

As early in the spring as weather conditions would permit field work the students were given a mimeographed schedule of observations and records that were to be made on field trips. Small groups of students were then taken into the field and together with the instructor observed and recorded a typical exposure of a succession of rocks of Pennsylvanian age found in a road cut near New Concord, Ohio. Each student contributed his observations, and the members of the group recorded the observations in their note-books. The instructor directed the activities and attention when necessary, making sure that all important points were observed.

After the group instruction in the field each student chose from a list of places previously selected by the instructor a road cut, ravine or roadside ditch near New Concord in which to observe and study a consecutive succession of rock exposures. The student was instructed to observe and describe the successive exposures and their contacts as carefully as possible and to collect whatever fossils they could find. The fossils which they collected were identified in the laboratory. Thus the field trip contributed to the work in the laboratory. When a student's observation was complete the record was presented to the instructor, who checked it for completeness and accuracy. In most cases it was necessary to send the student back over the area to make a more careful and detailed observation. All observations were to be completed and the records checked and accepted before the day on which the class discussion of the Mississippian period was finished.

On the day scheduled for the beginning of the class

[1] C. S. Gwynne, SCIENCE, November 11, 1938.

study of the Pennsylvanian period the selected sections described by the students were assembled and copied on the blackboard, and in so far as possible these sections were correlated. From these correlated sections, covering an area of about three square miles, a generalized cross section of the rocks of the New Concord region was made. This work was done largely by the students; the instructor, acting as a secretary, did the actual writing on the board.

From the information thus collected the class then reconstructed the geologic history of the region immediately surrounding New Concord. This offered an opportunity for the students to apply the scientific method in their study of the region. With the history of our own area in mind we then turned to the textbook for a more complete picture of the Pennsylvanian as a whole, keeping in mind the idea of tying up the region we had actually studied with the Pennsylvanian system as it is found in North America and tying the geologic history of the New Concord region as we had reconstructed it from our field study of the region with the history of the Pennsylvanian of North America.

This plan of procedure is not without its weaknesses, most serious of which is the fact that before the student starts out on his own to observe the rocks and record his observations he needs more field experience than we have given him. We plan to overcome this difficulty by beginning to observe and describe the rocks during the first semester in addition to the observation of the physical phenomena which heretofore has constituted most of our field work during the first semester. It is quite possible, too, that we will be able to find time for more than one conducted field trip early in the second semester field season before sending the student into the field on his own.

On the other hand, this procedure has several desirable features. The student develops a realistic idea of the Pennsylvanian and, indeed, the whole of the geologic column and of geologic history by actually studying, recording and interpreting his observations of a part of the rocks of the Pennsylvanian system. He arrives at a better appreciation of the work of the geologist through his own experience in working as the geologist works. His interest in geology is increased through active participation. He has had the experience of observing and recording evidence and in drawing inferences from the evidence. Thus he has actually had a concrete experience with the scientific method.

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## ENDOGONE AS ANIMAL FOOD

ALTHOUGH the genus Endogone has received comprehensive taxonomic treatment little is recorded of the rôle which species of these hypogeous fungi may play in the economy of nature. It is to be expected th[at] the small, truffle-like fructifications of *Endogone* mig[ht] be eaten by some animals, but accounts of their use [as] food seem strangely lacking. It seems in order, therefore, to place on record certain instances where su[ch] materials have been found in stomach contents [of] shrews and mice.

Dr. W. J. Hamilton in August, 1938, sent to th[e] U. S. Biological Survey specimens from Ithaca, N. Y. with the observation that "the small black objects... were often, but not invariably associated with earthworms in stomach contents" of *Blorina brevicauda*. The "small black objects" referred to the writer f[or] identification proved to be zygospores with the abundant hyphal network characteristic of *E. macrospora* Tul. It was suggested that the black zygospores wh[ich] often measured ¼ mm (250 μ) in diameter might ha[ve] been ingested first by the earthworms and secondari[ly] by the shrew. On consultation with Mr. H. C. Ga[...] of Washington, who has had a vast experience [in] cultivating earthworms, the information was elicite[d] that earthworms would have difficulty in swallowi[ng] refractory objects of that diameter and that he doubt[ed] the ability of any North American earthworms to inge[st] such material. It is, of course, likely that the shre[w] had developed a taste for this fungus as a condime[nt] with the pièce de résistance.

Dr. Hamilton in correspondence, furthermore, reported the finding of these black bodies in stoma[ch] contents of two other shrews (*Sorex fumeus* and *S. cinereus*) as well as of three woodland mice (*Peromyscus leucopus novoboracensis, Clethrionomys gapperi* an[d] *Synaptomys cooperi*) and pointed out that these fin[d]ings in the small rodents which very seldom feed [on] earthworms supported the assumption that the shre[ws] and mice may well have eaten the *Endogone* directl[y].

In this connection it is pertinent to note an old[er] record of such fungi in stomach contents of a mo[use] (*Synaptomys cooperi gossi*) as attested by preserv[ed] microscopic preparations on file in the Mycologic[al] Collections of the Bureau of Plant Industry. The[se] slides show zygospores of a distinctly different speci[es] of *Endogone* as yet undetermined specifically. T[he] specimens studied and recognized as *Endogone* in 19[..] by Miss V. K. Charles was collected by T. E. White [in] Douglas County, Kansas, in October, 1925, and examined first by C. C. Sperry, of the Biological Surv[ey] who found the total stomach contents to be *Endogo[ne]* 5 per cent. and finely chewed vegetation, probabl[y] grass, 95 per cent. This latter information has be[en] most kindly furnished by Dr. Clarence Cottam, of th[e] Survey. In this case it is also notable that there [is] no reference to any accompanying earthworms.

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## USCLE AND BLOOD HEMOGLOBIN IN THE DOLPHIN

OBINSON[1] has recently reported the muscle hemo-bin of harbor seals (*Phoca vitulina*) as being 7.715 per 100 gm of fresh tissue. We are reporting our ults for skeletal muscle and blood from dolphins *urciops truncatus*) studied during the past summer ough the courtesy of the Marine Studios of St. gustine, Florida.

Muscle and blood samples were obtained simulta-usly from a living female dolphin which weighed kg. Muscle hemoglobin was determined by the thod of Whipple[2] and compared colorimetrically h the blood hemoglobin.

The oxygen capacity of the blood was 19.1 volumes cent., or 14.25 gm hemoglobin per 100 cc. The oglobin content of the sacro-spinalis muscle was 34 gm per 100 gm tissue. The muscle hemoglobin centration in the dolphin is thus less than that nd in the seal by Robinson, but greater than that the dog (0.85 to 1.00 gm per 100 gm rectus ab-inis muscle).

It should be noted that the common submersion time the dolphin is rarely over a few minutes; therefore oxygen storage of the dolphin need not be as great that of the seal. It will also be necessary to deter-ne the amount of myoglobin in dolphin skeletal muscle in order to determine the oxygen storage more exactly; work on this problem is now in progress.

LILLIAN EICHELBERGER
EDWIN S. FETCHER
E. M. K. GEILING
BERT J. VOS[3]

UNIVERSITY OF CHICAGO

## BIOGRAPHY OF DR. HARVEY CUSHING

MRS. CUSHING has requested me to prepare a biography of her husband, and I should be most grateful to any one who wishes to make letters, anecdotes or other memorabilia available.

Copies of all letters, no matter how brief, are desired, and if dates are omitted it is hoped that, when possible, these may be supplied (*e.g.*, from the post-mark). If original letters or other documents are submitted, they will be copied and returned promptly.

A new Medical Library building is being erected at the Yale University School of Medicine to receive Dr. Cushing's library and collections, including his letters, diaries and manuscripts. Any of his friends who wish, now or later, to present correspondence, photographs or other memorabilia for permanent preservation among the Cushing papers will receive the appreciative thanks of the university.

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# SPECIAL ARTICLES

## HE ACTION OF CERTAIN HORMONES AS DIETARY CONSTITUENTS

THE present study was prompted by the following oretical consideration.[1] We know that normal food tains small quantities of hormonic substances, ich may exert certain activity and may perhaps be lized by the organism as precursors of other hor-nes. On the other hand, a deficient diet may lack tain building stones from which the animal organ-n synthesizes its own hormones.

Judging from our present knowledge, the various rmones belong mainly to three chemical classes, *viz.*, nple nitrogenous substances, derived mostly from the ino acids of the diet, hormones belonging to the roid group and finally hormones of protein nature. far as the first two groups are concerned, it is vious that the organism prepares these substances om material present in the food. More complicated the origin of activity of the protein hormones. ese substances when hydrolyzed do not seem to differ structure and composition from the usual proteins; no known protein exhibits any definite hormonal activity. Whether the hormonal action is associated with a definite constituent or whether this activity depends on certain spatial configuration of the amino acids, must remain unanswered for the present.

Further, it seems possible that on deficient diets, the synthetic capacity of the organism may become impaired, even though the actual precursors are present. It is hoped that further work will give an answer to the problems outlined.

The present study deals with the action of estrin, testosterone propionate and gonadotropic hormone (of pregnant mare serum)[2] when added to the diet. The problem was approached in this way: a diet was chosen which causes a definite retrogression of the organs to be studied; then a regeneration was sought by inclusion in the diet of the corresponding hormone. It was soon found out, however, that most of the problems raised require special dietary studies: for instance, a diet which is responsible for marked retrogression of the female sex apparatus exerts no influence on the corresponding organs of the male.

In order not to complicate our task, we have used

[1] D. Robinson, SCIENCE, 90: 276, 1939.
[2] G. H. Whipple, *Am. Jour. Physiol.*, 76: 693, 1926.
[1] The present work was outlined by the senior author an address given on November 10, 1938, at the Hotel erre, New York City.

[3] These names are listed alphabetically because the work was carried out by the authors as a group. No indication of seniority is implied.
[2] We are indebted for the hormones to Roussel Laboratory, Paris, and Dr. André Girard.

TABLE I

Experiments with Estrin*

| Diet | Nature of experiment | Number of animals | Duration days | Dose mg | Weight | Loss or gain per cent. | Food | Ovar. mg | Uteri mg |
|---|---|---|---|---|---|---|---|---|---|
| I | Controls ........ | 8 | 26 | | 920 | 0 | 1,595 | 541 | 897 |
| I | Estrin ......... | 8 | 26 | 17.6 | 928 | – 10.7 | 1,467 | 476 | 1,797 |
| I | Controls ........ | 8 | 34 | | 1,151 | + 2.5 | 2,307 | 458 | 971 |
| I | Estrin ......... | 8 | 34 | 10.27 | 1,126 | – 1.5 | 2,055 | 535 | 2,047 |
| I | Estrin plus Gonadotr. H. .... | 8 | 30 | 10.27 E 5.2 G. H. | 1,097 | + 0.4 | 2,021 | 555 | 1,674 |
| II | C. ............. | 8 | 33 | | 1,069 | + 11.8 | 2,221 | 765 | 1,907 |
| II | Estrin ......... | 8 | 33 | 6.3 | 1,049 | + 11.9 | 2,115 | 682 | 1,864 |

* The doses of hormones and other data are calculated for 8 rats for the whole period throughout all the tables.

largely a purified diet, to which only those vitamins were added which were available in a pure form. This procedure presented the disadvantage that the diet was incomplete and that the experiments had often to be interrupted before a complete exhaustion of the dietary reserves could be expected. This study was carried out on some 240 piebald rats and the composition of the diets used was as follows:

| | Diet I | Diet II | Diet III |
|---|---|---|---|
| Casein | Non-pur. 200 | Non-pur. 180 | Same as Diet I, but casein and starch washed with dil. HCl and extracted with alcohol. |
| Starch | " 500 | " 470 | |
| Lard | " 250 | " 250 | |
| Salts | 40 | 40 | |
| Cod liver oil | 20 | 15 | |
| Yeast | — | 60 | |
| Whole wheat | — | 200 | |
| Daily additions: | | | |
| $B_1$ | 5γ | | |
| Lactoflavin | 10" | | |
| Adenosine | 50" | | |
| Nicotinic ac. amide | 100" | | |

From the above results we may conclude that a deficient diet, as used above, produces a marked retrogression of female sex organs; and that this is definitely influenced by an oral administration of estrin. O less deficient diet (Diet II), retrogression does not tak place, and estrin *per os* has no effect. Estrin i female rats depresses the food intake and causes lo in weight. Simultaneous administration of estrin an gonadotropic hormone slightly inhibits the estri action on the uterus. The activity of estrin inco porated into a deficient diet, and its inactivity on more complete diet supports our view of the possib importance of this substance as a food constituent (a outlined in the introduction).

TABLE II

Experiments with Testosterone Propionate

| Diet | Nature of experiment | Number of animals | Duration days | Dose mg | Weight | Loss or gain per cent. | Food | Test. g | S.V. g |
|---|---|---|---|---|---|---|---|---|---|
| I | C. ....... | 3 × 8 = 24 | 39 | | 1,001 | + 3.9 | 2,308 | 24.8 | 2.08 |
| I | Testost. .. | 3 × 8 = 24 | 39 | 17.5 | 1,002 | + 0.6 | 2,500 | 24.0 | 2.2 |
| II | C. ....... | 8 | 40 | | 1,199 | + 43.4 | 3,593 | 23.9 | 7.9 |
| II | Testost. .. | 8 | 40 | 15.45 | 1,212 | + 52.7 | 3,716 | 24.4 | 8.5 |
| III | C. ....... | 8 | 28 | | 1,146 | – 24.1 | 1,719 | 22.4 | 1.0 |
| III | Testost. .. | 8 | 28 | 16.75 | 1,147 | – 14.8 | 1,820 | 26.4 | 1.8 |

In discussing the Tables II and III we may co clude that a diet which produces sex organ degenera tion in females, leaves the male practically untouche No changes take place unless the animals lose consid erable weight. The action of male and gonadotrop hormones seems to be fairly definite. In contrast t the estrin action in females, the male and gonadotrop hormones exert a rather beneficial action on the foo intake and weight, which is perhaps another eviden of their value as food constituents.

Having established that the degeneration of the ma sex organs takes place on purified casein and starch

TABLE III

Experiments with Gonadotropic Hormone

| Diet | Nature of experiment | Number of animals | Duration days | Dose mg | Weight | Loss or gain per cent. | Food | Test. g | S.V. g |
|---|---|---|---|---|---|---|---|---|---|
| I | C. ....... | 3 × 8 = 24 | 39 | | 1,001 | + 3.9 | 2,308 | 24.8 | 2.08 |
| I | G. H. .... | 3 × 8 = 24 | 39 | 22.3 | 1,008 | + 1.2 | 2,486 | 23.2 | 2.34 |
| III | C. ....... | 8 | 28 | | 1,146 | – 24.1 | 1,719 | 22.4 | 1.0 |
| III | G. H. .... | 8 | 28 | 16.75 | 1,147 | – 21.5 | 1,676 | 26.2 | 1.4 |

we have initiated dietary studies in this direction, keeping in mind, however, that the above effect might be due to loss in weight, rather than to dietary deficiencies.

TABLE IV

INFLUENCE OF DIET ON SEX ORGANS OF THE MALE

| Diet | Nature of experiment | Number of animals | Duration days | Weight | Loss or gain in per cent. | Food | Test. g | S.V. g |
|---|---|---|---|---|---|---|---|---|
| I | C. ......... | 8 | 39 | 1,314 | +11 | 2,449 | 23.7 | 5.75 |
| I | 60 g. yeast per kg food .... | 8 | 39 | 1,241 | +46 | 3.359 | 22.8 | 8.33 |
| I | 200 g. whole wheat added to kg food.. | 8 | 39 | 1,327 | +27 | 3,246 | 22.6 | 7.31 |
| I | C. ......... | 8 | 32 | 1.070 | – 6.3 | 1.977 | 26.9 | 1.5 |
| I | Casein extr.* | 8 | 32 | 1,069 | – 5.2 | 2.297 | 28.7 | 1.8 |
| I | C. ......... | 8 | 35 | 841 | + 9.5 | 1.844 | 26.2 | 1.24 |
| I | Casein extr.† | 8 | 35 | 834 | + 1.6 | 1,710 | 22.6 | 0.85 |

* Acetone, acid alcohol and aqueous HCl extract added to imperfectly purified casein.
† Acetone and alcohol extract added to imperfectly purified casein.

From the above table we gather that the nature of dietary additions plays an important role in maintaining the normal aspect of the sex apparatus of the male rat. Additions and extracts containing undefined substances of yeast, whole wheat and aqueous casein extracts exert a favorable action on the food intake and weight, as well as on the picture of the seminal vesicles. Contrary to this, the only experiment with fatty extract of casein was unfavorable in these respects.

Finally, experiments were performed for the purpose of ascertaining the action of synthetic estrogens (dihydro-stilbestrol) which have nothing in common in chemical structure to natural estrogens. Further, we investigated whether testosterone can replace estrin as a hormonic dietary precursor.

Both groups of rats receiving dihydro-stilbestrol in their food showed continuous estrus. The action was practically the same on an incomplete and on a more complete diet. This is in marked contrast to the estrin action, which is only evident on an incomplete diet. As compared with the controls, testosterone initiated in several instances the beginning of an estrus, but it could not be substituted as a dietary estrin precursor. Stilbestrol on a more incomplete diet was somewhat toxic, but less so on a more complete dietary. Testosterone acted adversely in female rats regarding the food intake and therefore weight.

On a deficient diet female sex organs undergo a marked retrogression with cessation of estrus. Inclusion of estrin in such cases shows evidence of definite activity. On the other hand, a more complete diet causes no retrogression and estrin activity is not noticeable. Dihydro-stilbestrol, on the contrary, exerted the same activity on both types of food. Testo-

TABLE V

ACTION OF DIHYDRO-STILBESTROL AND TESTOSTERONE PROPIONATE ON FEMALE RATS

| Diet | Nature of experiment | Number of animals | Duration days | Dose mg | Weight | Loss or gain per cent. | Food | Ovar. mg | Uteri mg |
|---|---|---|---|---|---|---|---|---|---|
| I | C. ....... | 8 | 34 | | 779 | – 8.9 | 1,183 | 294 | 542 |
| I | Stilbestrol. | 8 | 34 | 4.7 | 774 | –27.9 | 906 | 273 | 1,779 |
| I | Testost. .. | 8 | 34 | 9.1 | 777 | –12.1 | 1,143 | 315 | 541 |
| I | Stilbestrol. | 8 | 34 | 5.3 | 754 | – 5.8 | 1,319 | 369 | 1,716 |

SUMMARY

sterone can not replace estrin as a dietary hormonal precursor.

The sex organs of the male are more resistant to dietary deficiencies, the animals showing only retrogression along with a significant loss in weight. Testosterone and gonadotropic hormone (of pregnant mare serum) produce a small but definite restorative effect.

Oral administration of estrin to females depresses the food intake, while testosterone, and less so the gonadotropic hormone in males produces the opposite effect. This effect can be regarded as evidence of the dietary significance of these two hormones.

The expenses of the present investigation were defrayed by the U. S. Vitamin Corporation, of New York City.

CASIMIR FUNK
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CASA BIOCHEMICA,
RUEIL-MALMAISON, FRANCE

## THE EXCRETION OF CORTIN AFTER SURGICAL OPERATION

A METHOD for the extraction and determination of cortin in human urine has been described.[1] The determination is based on a biological assay for cortin described by Selye and Schenker.[2] Using the method in a study of a group of cases, including one appendectomy, one dilatation and curettage, two gastric resections and one colostomy (none of whom developed post-operative shock), it was found that after operation there is an increased amount of cortin in the urine. Two cases are illustrated in the accompanying table. The excretion of cortin increases to a maximum between the third and fifth post-operative day and then gradually declines to pre-operative levels.

It had previously been shown[1] that cortin appeared in the urine during convalescence from influenza in persons who normally excrete none and that in the presence of chronic suppurative infection cortin is

[1] P. Weil and J. S. L. Browne, Proc. Am. Physiol. Soc., Toronto, 1939, Vol. 121, p. 652.

[2] Hans Selye and V. Schenker, *Proc. Soc. Exp. Biol. and Med.*, 39: 518, 1938.

TABLE I

| Date | | Units |
|---|---|---|
| June 9 | | 0 |
| 10 | | 0 |
| 11 | | 0 |
| 13 | Operation-Colostomy | |
| 14 | | 25 |
| 15 | | 25 |
| 16 | | 50 |
| 19 | | 75 |
| July 2 | | 50 |
| 4 | | 25 |
| 6 | Operation-Gastrectomy | |
| 7 | | 75 |
| 9 | | 125 |
| 10 | | 125 |
| 11 | | 100 |
| 12 | | 50 |

excreted. We believe that the increased excretion of cortin is a manifestation of the response of the organism to a damaging stimulus by an increased secretory activity of the adrenal cortex. It has been shown that the adrenal cortex of the laboratory animal hypertrophies after damage.[3] These experiments and the present investigation suggest that an increased secretion of the adrenal cortical hormone forms part of the protective mechanism against damage.

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## PERIODIC MITOTIC ACTIVITY IN THE EPIDERMIS OF THE ALBINO RAT

THE knowledge that mitotic activity was periodic in some plants led Fortuyn-van Leyden to investigate this phenomenon first in various tissues of young kittens,[1] later, in young mice.[2] She found periods of maximum and minimum activity. Since then Ortiz Picón,[3] working with the epidermis of young mice, and Carleton,[4] studying the epidermis and hair follicles of young mice, have corroborated her findings as to periodicity, but have not agreed as to the time of maximum and minimum activity. More recently Cooper and Schiff[5] have demonstrated periods of greater and lesser mitotic activity in the epidermis of the prepuce of human male infants. The author[6] has reported a study of mitotic activity in the renal cortex of male albino rats. The curve plotted from the findings exhibited both periodic and rhythmic features (Fig. 1,

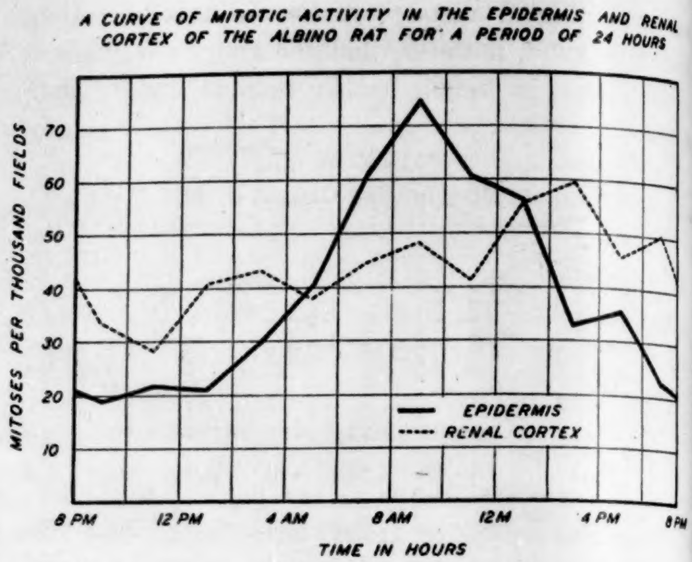


FIG. 1

broken line). Elliott,[7] as part of a study on the growth mechanisms of articular cartilage, obtained specimens during the day and night, but found no difference in rate of cell division.

The importance of such studies in the problem of normal and abnormal growth is obvious. The differences in results of various investigators may be due to the ages and orders of mammals employed, organ or region studied, inherited qualities or individual variation, character of environment or the small size of some of the samples. An addition to available data is here presented, a study of mitotic activity in the epidermis of the albino rat.

Materials and methods were as follows: from each of 96 male albino rats, 28 days old, killed in groups of 8 at intervals of 2 hours during a period of 24 hours, a square of skin was cut from the central ventral portion of the abdominal wall. The specimens were fixed in Bouin's, cross-sectioned at 8 microns, mounted serially and stained with hematoxylin and eosin Y. Every fourth section was studied to avoid counting the same mitosis twice. The number of mitoses observed in 1,000 consecutive fields was taken as an index of mitotic activity in a specimen. From the data obtained a curve was constructed and biometric studies made. To conserve space individual values are not presented.

The curve (Fig. 1, solid line) is composed of mean values for each 2-hour interval, placed at the mid-point of the interval. Each mean value is the average of 8 individual values. It will be seen that mitotic activity was greatest during the interval 8 A.M. to 10 A.M. (75 mitoses per 1,000 fields) and least during the interval 8 P.M. to 10 P.M. (19 mitoses per 1,000 fields); or, in other words, mitoses were almost 4 times as numerous in the morning interval as in the evening period. With few exceptions the skin was obtained from the same rats as were the kidneys previously studied. A

[3] Hans Selye, *Endocrinology*, 21: 169, 1937.

[4] Aided by a grant from the Banting Research Foundation.

[1] C. E. D. Fortuyn-van Leyden, *Proc. Akad. wet. Amsterdam*, 19: 38, 1917.

[2] C. E. D. Fortuyn-van Leyden, *Proc. Akad. wet. Amsterdam*, 29: 979, 1926.

[3] J. M. Ortiz Picón, *Zeitschr. f. Zellforsch. u. mikr. Anat.*, 23: 779, 1933.

[4] A. Carleton, *Jour. Anat.*, 68: 251, 1934.

[5] Z. K. Cooper and A. Schiff, *Proc. Soc. Exp. Biol. and Med.*, 39: 323, 1938.

[6] C. M. Blumenfeld, *Anat. Rec.*, 72: 435, 1938.

[7] H. C. Elliott, *Am. Jour. Anat.*, 58: 127, 1936.

comparison of the curve of mitotic activity in the epidermis with that of the renal cortex shows coincidence of the periods of minimum activity but an interval of 6 hours between periods of maximum activity. Nor does the curve for the epidermis have the rhythmic character of that for the renal cortex.

For biometric studies the 24-hour period was subdivided thus: first half of day, 8 A.M. to 2 P.M.; second half of day, 2 P.M. to 8 P.M.; first half of night, 8 P.M. to 2 A.M.; and second half of night, 2 A.M. to 8 A.M. Mitotic activity was found to be significantly greater during the first half of the day and significantly lower during the first half of the night than during the rest of the 24-hour period.

No explanation of these findings can be given as yet. If factors external to the cells have a part in determining periods of maximum and minimum mitotic activity they did not, in these animals, exert their influence in all parts of the body at the same time. A most valuable lead is furnished by the work of Huggins and Noonan[8] on the relation of temperature to red bone marrow activity and of Fay and Henny[9] and Smith and Fay[10] on the relation of temperature differences to normal and abnormal growth. This is one direction in which the present work is being continued.

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## SCIENTIFIC APPARATUS AND LABORATORY METHODS

### A DEVICE FOR RAPID RINSING OF ABSORPTION TOWERS USED IN GAS ANALYSIS STUDIES[1]

Where an assembly of several glass absorption towers are employed for carbon dioxide or other gas determinations as, for example, in case of the Heinicke and Hoffman[2] photosynthesis apparatus, there is a special need for rapid and efficient rinsing of the towers after each determination. The simple device described below has these two advantages.[3] The whole system can be made from standard glassware in about a half day. The time necessary for each rinsing of the towers is reduced by more than one-half.

Details of this device, which has been used successfully for several months, are clearly shown in Fig. 1. The rinse water can be made to flow under pressure by connecting a blower pump or air-pressure line at A and applying pressure in the 10-gallon carboy, B, until the mercury in the manometer, C, indicates a level differential of about 12 inches. The pinch clamp, F, is a safety clamp employed between rinsings. It aids also in directing distilled water to the stationary stock water bottle, D, from the portable bottle, N. The same source of air pressure used at A can be attached at M, to force the water from bottle, N, to bottle D.

To rinse the towers after a determination, clamp F is released first (clamp G is open only during the filling of bottle D),[4] then clamp H is released with the left hand and clamp I (to another pair of towers) is

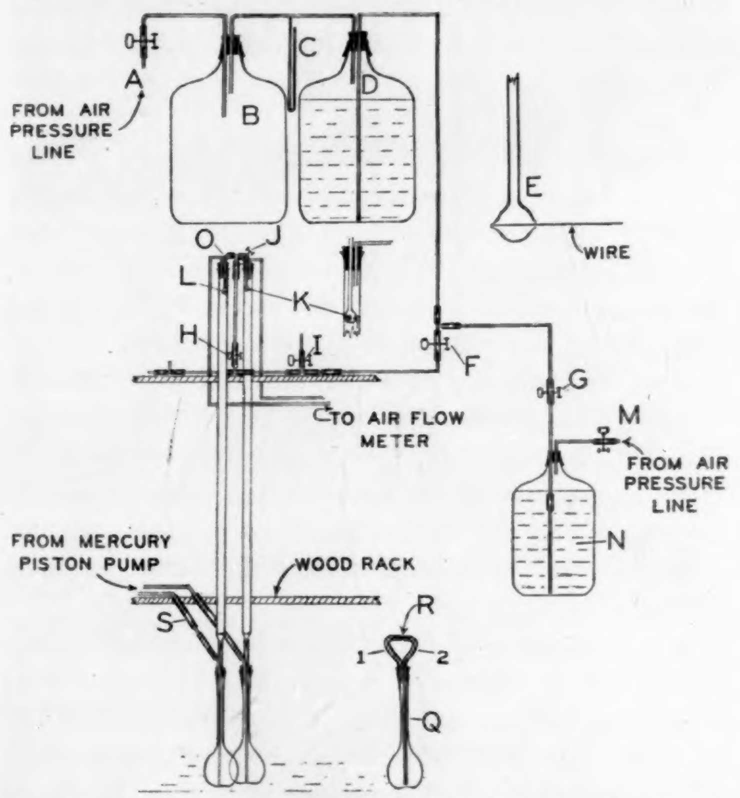


Fig. 1. Diagram showing system employed for rapid rinsing of gas-absorption towers.

released with the right hand. This allows the distilled water under pressure to squirt through the syringe-like bulbs at K and L as well as through the bulbs in another set of towers which is connected to the system at I. Thus, a set of four towers can be washed at one time. The water will flow evenly down the sides of the towers, provided they have been thoroughly cleaned in the beginning with a strong cleaning solu-

1 The authors are indebted to the Sherwin-Williams Paint Company, under whose fellowship part of this information has developed, and to F. W. Southwick, graduate assistant in horticulture, for helpful suggestions.

2 A. J. Heinicke and M. B. Hoffman, Science, 77: 55–58, 1933.

3 The removal and replacement of stoppers at the top of towers before and after rinsing is not necessary. They may be securely set and sealed about the edges with a mixture of grafting and sealing wax to obviate possible leakage of air at this point.

8 C. Huggins and W. J. Noonan, *Jour. Exp. Med.*, 64: 275, 1936.

9 T. Fay and G. C. Henny, *Surg., Gynec. and Obstet.*, 66: 512 (no. 2A), 1938.

10 L. W. Smith and T. Fay, *Jour. Am. Med. Asn.*, 113: 653, 1939.

4 Clamp J should be closed when air-flow records are taken. This prevents back-pressure from one tower to another of a pair.

tion to remove waxy and oily films, and provided the four or five perforations in each bulb are approximately the same size. The glass tubing used for the main water lines should be about 9 mm outside diameter, while leads to the individual towers may be smaller in diameter or about 7 mm outside diameter.

The bulbs, one of which is described at K, can be made easily without special technique in glass blowing. The following procedure is suggested: Heat the end of a five-inch glass tube which is approximately 7 mm in diameter until it has sealed; remove from the flame and blow immediately a bulb on the end, which is about one half inch in diameter. Allow to cool; heat again one side of the bulb and blow a pimple. Heat another side at a right angle to the first; blow another pimple and with a file gently file two holes at these points. The last two or three holes can be made quickly by inserting a rigid wire through the first holes and pushing out pimples on individually heated sides of the bulb, as shown at E. These pimples are filed off and the holes fire-polished.

Sometimes difficulty is encountered with loss of solution by bubbling over the tops of the towers, especially when about two drops of n-butyl alcohol[5] have been added to every 100 cc of alkali solution to increase the number of bubbles and decrease their individual size. When the solution in a tower threatens to overflow at the beginning of a run, this may be checked by removing the rubber tubing at 0 and with a medicine dropper allowing about two drops of capryl alcohol to settle to the base of the bulb. Capryl alcohol has the reverse effect of butyl alcohol on surface tension. When a mass of bubbles strikes the bulb, the foam immediately falls back.

The diagram at Q demonstrates how the rubber tubing on the two arms of a flask may be sealed from outside air before and after it is attached to the apparatus. This eliminates the expense and awkwardness of pinch-clamps. The three-inch glass tube, R, should be inserted further in the rubber tubing of arm 1 than arm 2. It thus will consistently, pull out of arm 2 more easily than arm 1, and will be ready for the rubber connection, S.

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## A NEW CULTURE MEDIUM FOR PARAMECIA

VARIOUS devices have been suggested for slowing down and entangling Paramecia for microscopic study. The most satisfactory appears to be the addition of a small amount of fine cultural debris to the drop of medium on the slide. Cultures made up of hay infusions contain relatively little fine material. In order to increase the amount of fine debris we use the following method of raising Paramecia. 0.2 gram "Pablum" (an infant food manufactured by Mead Johnson and Company) is added to 400 cc of tap water in a wide mouth pint jar. This is covered by an inverted glass coaster and autoclaved at 15–20 pounds steam pressure for 30 minutes. After the mixture has cooled it is inoculated with Paramecia and allowed to stand at room temperature. In a week's time a dense culture of Paramecia is obtained. The "Pablum" concentration given above seems to be optimum.

To dispense the Paramecia to students we usually stir up the contents of a culture jar for a uniform distribution of Paramecia and fine cultural debris. On microscopic examination we find that most of the Paramecia are feeding and therefore easier to study. When greater concentrations of Paramecia are desired on a slide an unagitated drop of medium from the surface where the Paramecia aggregate, together with a small amount of debris from the bottom, may be used. Ordinarily one such culture as described above suffices for a hundred or more students.

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[5] M. D. Thomas, *Ind. Eng. Chem., Anal. Ed.*, 5: 193–8, 1933.

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